CXCL12 Signaling Is Essential for Maturation of the Ventricular Coronary Endothelial Plexus and Establishment of Functional Coronary Circulation.

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Authors: Susana Cavallero, Hua Shen, Christopher Yi, Ching-Ling Lien, S Ram Kumar, Henry M Sucov

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Public Summary:
This study explored the role of the protein CXCL12 (also called SDF1) in supporting the formation of coronary blood vessels in the embryonic heart. The study demonstrated that CXCL12 is required for coronary vessel development, specifically to instruct newly forming vessels whether to become arteries or veins. In this evaluation, the broader role for coronary vessels in heart development could also be understood.

Scientific Abstract:
Maturation of a vascular plexus is a critical and yet incompletely understood process in organ development, and known maturation factors act universally in all vascular beds. In this study, we show that CXCL12 is an organ-specific maturation factor of particular relevance in coronary arterial vasculature. In vitro, CXCL12 does not influence nascent vessel formation, but promotes higher-order complexity of preinitiated vessels. In the heart, CXCL12 is expressed principally by the epicardium, and its receptor CXCR4 is expressed by coronary endothelial cells. CXCL12 is not a chemotactic signal for endothelial cell migration, but rather acts in a paracrine manner to influence the maturation of the coronary vascular plexus. Mutants in CXCL12 signaling show an excess of immature capillary chains and a selective failure in arterial maturation, and become leaky with the onset of coronary perfusion. Failed maturation of the coronary system explains the late-gestation lethality of these mutants.